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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/633,697	08/07/2000	Gerard Andrew Potter	A33403PCT USA-A	3756

21003 7590 04/23/2003

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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	20

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/633,697	POTTER ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *60-62* is/are allowed.

6)☒ Claim(s) *12-76,78,79,81 and 83-86* is/are rejected.

7)☒ Claim(s) *65,67,68,70,77,80 and 82* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to amendments filed on 2/24/03. Applicant has cancelled all pending claims. Claims 58-86 are new. Claims 43, 45, 46, and 48 had been found to contain allowable subject matter. There are twenty-nine claims pending and twenty-nine under consideration. Claims 58-70 and 75-82 are compound claims. Claims 71 and 83 are composition claims. Claims 72 and 84 are method of preparation claims. Claims 73, 74, 85, and 86 are use claims. The application concerns some benzyl and cinnamyl carbamate prodrug molecules. This is the third action on the merits.

Claim Objections

2. Objection is made to claims 65, 67, 68, 70, and 75-86 under 37 CFR 1.75 as being a duplicate of claims 58, 59, 60, 61, 63, 64, 58, 66, 59, 60, 69, 61, and 71-74 respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The phrase "according to claim 66" or "A CYP1B1 substrate" does not further limit the structure of the claimed compounds. They are completely defined by the structural formulas given in each claim. Thus, claim 65 is a compound claim with the same limitations as claim 58, i.e. a Markush group of two defined species.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The first and third formulas in this claim define the same molecule. What is intended by having slightly different representations of the same substance? The Examiner suggests deleting either formula (XV) or (XVII).

4. Claims 59, 67, and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each claim contains the phrases "in Formula XVIII" *etc*. These are indefinite for two reasons. Firstly, according to the MPEP §2173.05(s) "[w]here possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than

duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609. Secondly, the three radicals R_2, R_3, and X are completely defined. The Examiner can see no limitations that three phrases add. The Examiner suggests deleting the phrases.

5. Claims 63, 64, 66, 69-76, 78, 81, and 83-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The structural element in the formula of claims 63 and 75, "Chemical moiety"" is indefinite. Names, structures, and chemical formulas precisely define organic molecules. This limitation does not even define a chemical structure by any biological property. Claims where only a portion of the structure is defined are indeterminate in scope. They are allowed only when it is clear from the specification what substituents are intended and that they would not change the character and properties of the core. In *Ex parte DIAMOND*, 123 USPQ 167 the Board of Patent Appeals and Interferences, citing previous court decisions wrote, "We also direct appellant's attention to *Ex parte Ritter et al.*, Patent File 2,631,152, wherein we affirmed a rejection of claims specifying "a substituted guanyl urea" as too broad and indefinite." In the present case, Applicants have defined the

substituent, but fail to define the core chemical moiety. At one level the structure of the claimed radical is easy enough to understand. One simply takes every one of the forty million chemicals described in Chemical Abstracts, removes a single hydrogen atom from anywhere from each compound, attaches Applicants' carrier framework, and repeats the process with every hydrogen atom in every compound. Repeating the process with all forty million compounds defines the scope of the claim. However, the second paragraph requires Applicants to particularly point out and distinctly claim.

6. Claims 63, 64, 66, 69-76, 78, 81, and 83-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. What chemical structures are intended by the chemical radical "Chemical moiety"? The MPEP states in §2162 I.A. that "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." As explained above use of the word "Chemical moiety" as a chemical radical does not meet either of these tests. The MPEP states in §2162

II.A.(a), that "[p]ossession may also be shown by a clear depiction of the invention in detailed drawings or in ***structural chemical formulas*** (emphasis added) which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention."

7. Claims 63, 64, 66, 69-76, 78, 81, and 83-86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds where "Chemical moiety" has some therapeutic activity, does not reasonably provide enablement for using the compounds where "Chemical moiety" does not have such activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Examiner can neither find in the specification nor think of any reason inactive molecules would be linked to Applicants carrier framework.

8. Claims 63, 64, 66, 69-76, 78, 81, and 83-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. Instructions of how to search for Applicants' molecules hardly constitute

instructions to the skilled process chemist of how to synthesize such molecules. Trial and error is hardly adequate instructions.

9. Claims 72, 74, 84, and 85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific cancers of claims 74 and , does not reasonably provide enablement for "inhibiting tumor cell growth" generally. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

To make clearer the lack of enablement for treatment of all cancer, extrinsic evidence is supplied by Draetta (Ann. Reports Med. Chem.), final sentence on page 246 "[a]lthough many still think about the need for a magic bullet as a cure for all cancers, our knowledge of the molecular mechanism underlying this disease make the prospect of developing such a universal cure very unlikely." Since no universal cure for cancer has been developed, it follows that there is no correlation between the assays relied upon by applicants and the ability to treat all cancers. Thus, those assays are not sufficient to enable such claims.

The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "tumor" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular cancer would be treatable with Applicants' compounds would require clinical trials in each disease with each compound. Considering the billions of compounds covered by claim 63 and the multitude of different cancers, this is an enormous amount of experimentation. b) The direction concerning cancer treatment is found in Applicants' *in vitro* assay described in the paragraph spanning pages 19 and 20. In this passage Applicants'

describe testing the compounds of their invention against a cell line V79mzhulB1 but it is unclear if this cell line is related to any specific tumor. Applicants disclose data on two compounds of claim 1 in Table 1 on page 35. Applicants describe no formulations, doses, or dosing schedules required to practice their invention. c) There is no working example of cancer treatment in man or animal in the specification. d) The claims rejected are drawn to clinical medicine and are therefore physiological in nature. e) The state of the art in cancer therapy is summarized above. f) The artisan using Applicants invention would be a Board Certified physician in oncology with an MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the billions of compounds of claim 63 I as well as the presently unknown list of different cancers embraced by claim 73. Thus, the scope of the claims is huge.

Allowable Subject Matter

10. Claims 60-62 are allowed. The following is a statement of reasons for the indication of allowable subject matter: The transitional phrase "A prodrug" is a statement of intent and given no patentable weight. The Examiner has no opinion

if, the claimed molecules, are, in fact, prodrug molecules. Claims 58 and 59 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for after final amendments is (703) 872-9307. The Examiner is available from 8:30 to 5:30, Monday through

Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

mukund J. Shah

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

TCMcK
April 20, 2003